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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/821,155 | 04/08/2004 | Tibor Sipos | TS-008(CIP) | 9572 |

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The Law Office of Imre Balogh
276 Smith School Road
Perkasie, PA 18944

| EXAMINER | |
|---|---|
| HANLEY, SUSAN MARIE | |
| ART UNIT | PAPER NUMBER |
| 1651 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 04/19/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/821,155 | SIPOS ET AL. | |
| | Examiner | Art Unit | |
| | Susan Hanley | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7,22-27 and 42-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,22-27 and 42-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicants' amendment and remarks filed 12/29/06 are acknowledged.

Claims 1-7, 22-27 and 42-48 are under examination.

### *Terminal Disclaimer*

The terminal disclaimer filed on 12/29/06 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent Nos. 5,750,104; 5,324,514; 5,460,812; and 5,578,304 has been reviewed and is accepted. The terminal disclaimer has been recorded.

### *Claim Rejections - 35 USC § 103*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3, 6, 22, 23, 26, 44, 45 and 48 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sipos (US 5,750,104) in view of Sherman et al. (2000).

Applicants argue that Sipos does not teach that his composition can be used in combination with a protease inhibitor and that Sherman et al. take the "shotgun" approach by listing many medicaments for the treatment of PI-induces diarrhea. Applicants conclude that the combination of the two reference does not reach the level of obviousness to negate patentability. Applicants summarize Sherman at page 909, second column, and assert that the claimed combination of High Activity Antiretroviral drugs with an enteric-coated buffered composition is not suggested by the Sherman et al. reference. Applicants argue that Sherman et al. report that some efficacy has been

shown for treatment of PI-associated diarrhea with oat bran, etc.. Applicants quote from Sherman et al. at column 2, page 909, first full paragraph, to argue that "treatment of PI-associated diarrhea is 'largely non-specific and anecdotal, ranging from over-the-counter remedies to prescription drugs such as pancreatic enzymes." Applicants acknowledge that it "appears from Table 1 (p. 910) that all the listed medicaments used against PI-associated diarrhea has some beneficial effects but point out that each of the commonly used medicaments for the treatment of diarrhea is discussed under separate headings. Applicants argue that based on the teachings of the reference, any of the above-listed medicaments could be experimented with to treat PI-induced diarrhea," and assert that experimentation is not a standard by which to judge patentability.

Applicants argue that "In a rejection under 35 U.S.C. §103, it is fundamental that all elements recited in a claim must be considered and given effect in judging the patentability of that claim against the prior art. See In re Geerdes, 491 F.2d 1260, 1262-63, 180 USPQ 789, 791 (CCPA 1974). Thus, a case of obviousness is established by showing that some objective teaching or suggestions in the applied prior art taken as a whole and/or knowledge generally available to one of ordinary skill in the art would have led that person to the claimed invention, including each and every limitation of the claims, without recourse to the reaching in appellants' disclosure. See generally In re Oetiker, 977 F.2d 1443 at 1447-48, 24 USPQ2d 1443 at 1446-47. The prior art as applied must be such that it would have provided one of ordinary skill in the art with both a suggestion to carry out applicant's claimed invention and a reasonable expectation of success in doing so. See In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 fled. Cir. 1988). "Both the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure". Id.

Applicant argues that there is neither the suggestion or the expectation of success is contained in the cited Sherman reference and the Examiner is employing hindsight by using the appellants' disclosure as a blueprint to reconstruct the claimed invention from the isolated teachings of the prior art. See, e.g., Grain Processing Corp. v America Maize-Products Co., 840 F.2d 902, 907, 5 USPQ2d 1788, 1792 (Fed. Cir. 1988).

Applicants argue that a pH of 7 to 9 is required in the small intestine to release the buffering agent from the enteric coated composition and rendering the lipase and colipase, biologically active and that such specificity is not suggested by the Sherman et al. reference. Applicants note that in the Sherman et al. reference the pancreatic enzyme is administered per se, as it is, and is dissolved in the acidic environment of the stomach while Applicants' enteric coated enzyme along with the buffer does not dissolve in the stomach, it dissolves in the small intestine having a pH of 7 to 9 and this pH is insured by the presence of a buffeting agent in the enteric coated composition.

Applicants' arguments filed 12/29/06 have been fully considered but they are not persuasive. In response to Applicants' argument that there is no suggestion to combine the references and that Sherman provides an obvious to try motivation for reducing diarrhea and/or steatorrhea in a HIV-positive patient by administering to said HIV-positive patient the claimed medicament to treat diarrhea and/or steatorrhea in addition to the anti-retroviral drug (e.g., a protease inhibitor), the Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5

USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Applicants correctly point out that Sherman teaches using pancreatic lipase preparations that lack a buffer and enteric coating to treat diarrhea and/or steatorrhea in HIV-positive patients who are taking a protease inhibitor. Additionally, Sherman establishes that using such commercial preparations of digestive enzymes that lack the advantage of a buffer and enteric coating still significantly decrease the incidence of PI-induced diarrhea. *Sipos provides a generic teaching that it was a long sought need in the medical community to provide enzyme-containing digestive aids that would prevent gastric acid and pepsin inactivation of the enzymes upon passage through the stomach and then from the stomach to the duodenum in a predictable manner* (col.2, lines 19-29). Sipos teaches a composition of pancreatic enzymes that comprises a buffer and is enterically coated for the purpose of meeting this longstanding need. The composition of Sipos is identical to the instantly claimed composition. Sipos proves that his buffered, enterically coated composition is superior the prior art commercial preparations (which are the same as those disclosed by Sherman for successfully treating PI-induced diarrhea) for improving stool bulk and decreasing diarrhea (Table VII). Thus, the combination of the references teaches all of the claimed elements and provides motivation that is not "obvious to try." The ordinary artisan would have been motivated to substitute the composition of Sipos for the commercial digestive enzyme preparations taught by Sherman to treat PI-induced diarrhea and/or steatorrhea because the composition of Sipos was shown to be superior to the commercial preparations for relieving diarrhea and/or steatorrhea due to the protection of the digestive enzymes by the buffer and enteric coating. The desire to improve a result with a superior formulation of the active components (the digestive enzymes in the instant case) does not rely on an obvious to try motivation because the

prior art as a whole suggests that improvement in such treatment is desirable. The ordinary artisan would have had a reasonable expectation that the formulation of Sipos would serve as a successful replacement for the commercial digestive enzyme preparations because Sipos demonstrated that digestive enzyme preparations that are augmented by a buffer and enteric coating were superior to decrease the incidence of diarrhea and improve stool quality for digestive disorders.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

At the top of page 26 of the remarks filed 12/29/06, Applicants make a reply to the following rejection:

"Claims 1-3, 6, 8-12, 22, 23, 26, 28-32, 41, 45 and 48 are rejected under 35 U.S.C. §103(a) as being unpatentable over Sipos ('104) in view of Sherman et al., and further in view of Stuyver (U.S. 2003/0225029) and Hetherington et al., (U.S. 2003/003/0096274)."

This recitation of rejections based on 35 USC 103 does not appear in the Office action of 10/6/06. Hence, it will not be addressed.

Claims 1-6, 22-26 and 44-48 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sipos (US 5,750,104) view of Sherman et al. (2000) as applied to claims 1-3, 6, 22, 23, 26, 44,

45 and 48 above, and further in view of Stuyver (US 2003/0225029) and Hetherington et al. (US 2003/0096274).

Applicants state the basis of the rejection: "Sipos does not teach that the composition or method of use thereof, comprises a protease inhibitor that is a nucleoside reverse transcriptase inhibitor, as in claim 3, or a non-nucleoside reverse transcriptase inhibitor, as in claim 4." Applicants then recite the teaching of Stuyver and Hetherington. Applicants final statement regarding this rejection is that "Canani and Caskin are cited to suggest the rejection."

Applicants' arguments filed 12/29/06 have been fully considered but they are not persuasive because they do not address the factual bases of the rejection. Canani and Caskin are not cited in this rejection.

Claims 1-3, 6, 7, 22, 23, 26, 27, 42-45 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sipos (US 5,750,104) in view of Sherman et al. (2000) as applied to claims 1-3, 6, 22, 23, 26, 44, 45 and 48 above, and further in view of Canani et al. (1999) and Gaskin et al. (1982).

Applicants recite a passage of Canani on page 309-310, and assert that the passage would not provide encouragement to one skilled in the art to combine the teachings of the reference with Sherman. Applicants acknowledge that colipase increases lipase activity but argue that the references do not suggest the use of colipase in the present invention with an enteric-coated buffered composition. Applicants assert that present invention overcomes the drug-induced diarrhea and that the newly amended claims specify that the HIV-positive patient drug is dissolved in the acidic environment of the stomach and that the buffered enteric-coated composition is being dissolved in the small intestine having a pH of 7 to 9. Applicants state that they do not disagree

with the listing by the Examiner that lamivudine, didanosine and abacavir cause diarrhea in patients. However, Applicants argue that their invention is not to describe what causes diarrhea and steatorrhea, but to treat these conditions. Applicants assert that the references do not address what Applicants address, i.e., the treatment of these conditions.

Applicants' arguments filed 12/29/06 have been fully considered but they are not persuasive. Responding to Applicants' quotation of the passage from Canani and its relationship to Sherman, Applicants have not clearly pointed out what they are drawing on from Canani to form their conclusion that the skilled artisan would not combine the teachings of Canani with those of Sherman. The quotation of a passage does not prove a point unless Applicant addresses their interpretation of said passage and its relationship to their argument. Presumably, the passage is quoted to point out the uncertainty of the cause of fat malabsorption. However, this alleged uncertainty of the cause of fat malabsorption is not relevant to the rejection. The fact is that the result of HIV therapy is known: it negatively affects fat absorption. Hence, the reason for the study of Canani: a medication trial for children with HIV with the intention of improving gastrointestinal function that had been negatively affected by protease inhibitor therapy. The ordinary artisan, in this case a medical doctor, knows that she or he can prescribe drugs without understanding the precise etiology of a disease state.

The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In

this case, it is known from Sherman that HIV patients who experience diarrhea and/or steatorrhea experience relief from these conditions due to the enzymatic activity of the pancrelipase and that it is desirable to maximum concentration of the enzymes rapidly. As previously discussed, the addition of a buffer and enteric coated to the pancrelipase is an improvement over a known therapy. Similarly, the combined disclosure by Gaskin and Canani shows that the administration of colipase increases pancreatic actiivty. Thus, the addition of colipase to the composition of Sipos for the claimed method is another instance of improving the performance of a prior art composition with an agent (i.e. colipase) that will predictably increase the enzymatic activity of pancrelipase thereby increasing the efficacy of the composition in the claimed method.

Responding to Applicants assertion that present invention overcomes drug-induced diarrhea and that the newly amended claims specify that the HIV-positive patient drug is dissolved in the acidic environment of the stomach and that the buffered enteric-coated composition is being dissolved in the small intestine having a pH of 7 to 9, a close reading of the claims filed 12/29/06 does not demonstrate an amendment regarding the dissolution of the HIV drug and the buffered enteric-coated composition. The claim amendments dealt with the deletion of "preventing" language and the use of "co-lipase." As previously discussed, the addition of a buffer and enteric coated to the pancrelipase is an improvement over a known therapy.

Responding to Applicants' statement that "their invention is not to describe what causes diarrhea and steatorrhea, but to treat these conditions and the references do not address what Applicants address, i.e., the treatment of these conditions," this argument fails to comply with 37 CFR 1.111(b) because it amounts to a general allegation that the claims define a patentable invention

without specifically pointing out how the language of the claims patentably distinguishes them from the references.

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Hanley
Patent Examiner
Art Unit 1651

Leon B. Lankford, Jr.
Primary Examiner
Art Unit 1651